MM-181

# CARTITUDE-1: Two-year Post Last Patient In (LPI) Results from the Phase 1b/2 Study of Ciltacabtagene Autoleucel (Cilta-cel), a B-cell Maturation Antigen (BCMA)-Directed Chimeric Antigen Receptor T (CAR-T) Cell Therapy, in Patients with Relapsed/Refractory Multiple Myeloma (RRMM)


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## INTRODUCTION

- Ciltacabtagene autoleucel (cilta-cel; JNJ-68284528) is a chimeric antigen receptor (CAR)-T cell therapy for the treatment of patients with relapsed/refractory multiple myeloma (RRMM)[1]
- In the phase 1b/2 CARTITUDE-1 study, early, deep, and durable responses were observed with a single cilta-cel infusion in heavily treated patients with RRMM[1]
  - At a median follow-up of 21.7 months, responses were deepening and durable, with an overall response rate (ORR) of 98% and 82.5% of patients reaching stringent complete response (sCR)[2]
  - Median progression-free survival (PFS) and overall survival (OS) were not reached
- Cilta-cel was recently approved by the US Food and Drug Administration for the treatment of adult patients with RRMM after ≥4 prior lines of therapy (LOT), including a proteasome inhibitor (PI), an immunomodulatory drug (IMiD), and an anti-CD38 monoclonal antibody (mAb)[3]
- The Committee for Medicinal Products for Human Use of the European Medicines Agency has recommended cilta-cel for authorization in patients with ≥3 prior LOT[4]
- Here, we report landmark 2 years post last-patient-in results from the CARTITUDE-1 study with a longer duration of follow-up of 27.7 months

## METHODS

### Primary endpoints

- Phase 1b: Characterize the safety of cilta-cel and confirm the recommended phase 2 dose
- Phase 2: Evaluate the efficacy of cilta-cel

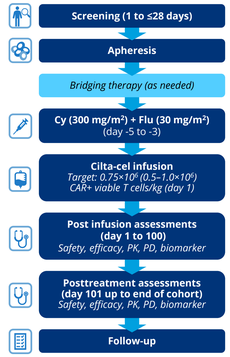
### Key eligibility criteria

- Progressive MM per International Myeloma Working Group criteria
- Eastern Cooperative Oncology Group performance status ≤1
- Measurable disease
- ≥3 prior LOT or double refractory
- Prior PI, IMiD, and anti-CD38 mAb exposure

### Median administered dose

- 0.71x10$^6$ (range 0.51–0.95x10$^6$) CAR+ viable T cells/kg

**FIGURE 1: CARTITUDE-1 study design**




Cy, cyclophosphamide; Flu, fludarabine; PD, pharmacodynamics; PK, pharmacokinetics

MULTIPLE MYELOMA

## RESULTS

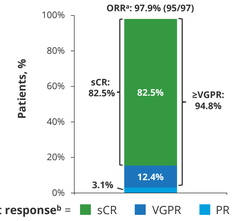
### Study population

- As of January 11, 2022, 97 patients were treated with cilta-cel with a median follow-up of 27.7 months
- Patients had received a median of 6.0 (range, 3–18) prior LOT
- Patient demographics and baseline characteristics have been previously described[1,2]

### Efficacy response

- ORR was 97.9% (95% CI, 92.7–99.7; **Figure 2**)
  - 82.5% (95% CI, 73.4–89.4) achieved sCR
- Responses deepened over time from the 12-month follow-up[1]

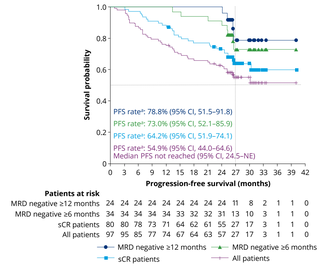
**FIGURE 2: Overall response rate**




[a]ORR assessed by independent review committee. [b]No patient had CR or stable disease. *CR*, complete response; VGPR, very good partial response

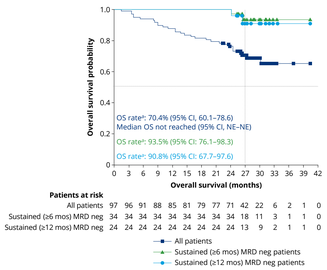
- Median duration of response (DOR) was not estimable (95% CI, 23.3 months–NE)
- Most patients in high-risk subgroups responded (ORR range 95.1–100%), including those with high-risk cytogenetics, high tumor burden (≥60% bone marrow plasma cells), and baseline plasmacytomas
- DOR, PFS, and/or OS were shorter in subgroups with high-risk cytogenetics, ISS stage III, high tumor burden, and presence of plasmacytomas
- High efficacy response rates were achieved despite a lack of detectable CAR-T cell persistence in peripheral blood following infusion among patients with 6 months of follow-up[1]
- Of 61 patients evaluable for minimal residual disease (MRD), 91.8% were MRD negative (10$^{-5}$) at a median follow-up of 27.7 months
- Patients with sustained MRD negativity (10$^{-5}$) for ≥6 and ≥12 months had improved PFS compared with the overall population (**Figure 3**)
- Median PFS and OS were not reached (**Figures 3 and 4**)
  - 54.9% of patients are still progression free and alive at 27.7 months (95% CI, 44.0–64.6)
  - Patients who achieved sCR had improved PFS compared with the overall population (**Figure 3**)

**FIGURE 3: Progression-free survival**




[a]27-month PFS rate.

**FIGURE 4: Overall survival**




[a]27-month OS rate.

### Safety

- The safety profile was manageable
- There were no new treatment-related deaths **(Table 1)**
  - A total of 30 deaths occurred during the study after cilta-cel infusion
  - No deaths occurred within the first 30 days, 2 occurred within 100 days, and 28 occurred >100 days post infusion

**TABLE 1: Deaths**

| | Total (N=97) | Time of death post cilta-cel infusion (days) |
|---|---|---|
| Total deaths during the study | 30 | 45–917 |
| Due to progressive disease | 14 | 253–746 |
| AEs unrelated to treatment (n=10) | | |
| Pneumonia | 1 | 109 |
| Acute myeloid leukemia[a] | 3 | 418, 582, 718 |
| Ascites[b] | 1 | 445 |
| Myelodysplastic syndrome | 1 | 803 |
| Respiratory failure | 3 | 733, 793, 829 |
| Septic shock | 1 | 917 |
| AEs related to treatment (n=6) | | |
| Sepsis and/or septic shock | 2 | 45, 162 |
| CRS/HLH | 1 | 99 |
| Lung abscess | 1 | 119 |
| Respiratory failure | 1 | 121 |
| Neurotoxicity | 1 | 247 |

[a]One patient with AML also had MDS and a cytogenetic profile consistent with MDS (del20q [present before cilta-cel infusion], loss of 5q); another patient who died from AML had both prostate cancer and squamous cell carcinoma of the scalp. [b]Patient died from ascites unrelated to cilta-cel as assessed by the investigator due to noncirrhotic portal fibrosis and nonalcoholic steatosis that was present for many years preceding the study. AE, adverse event; AML, acute myelogenous leukemia; CRS, cytokine release syndrome; HLH, hemophagocytic lymphohistiocytosis; MDS, myelodysplastic syndrome

- A total of 20 secondary primary malignancies were reported in 16 patients
  - Nine patients with hematologic malignancies (1 low-grade B-cell lymphoma, 6 MDS, 3 fatal AML [one patient had both MDS and fatal AML])
  - One patient each with malignant melanoma, adenocarcinoma, myxofibrosarcoma, and prostate cancer
  - Six non-melanoma skin cancers
- One new case of signs and symptoms of parkinsonism (previously termed movement and neurocognitive treatment-emergent AEs) (total n=6)
  - On day 914, patient experienced cognitive slowing, gait instability, and neuropathy (all grade 1), and tremor (grade 3); he is currently stable and functioning and remains in sCR
  - Had 2 risk factors for parkinsonism (grade 2 CRS and grade 3 immune effector cell-associated neurotoxicity syndrome) after cilta-cel[5,6]
- Following implementation of patient management strategies, the incidence of parkinsonism has decreased from 6% in CARTITUDE-1 to <0.5% across the CARTITUDE program[6]
- Three of the 6 total patients with parkinsonism have died (two from other underlying causes [sepsis and lung abscess] and 1 related to parkinsonism)
- Of the other two who are living, one has recovered, and one is recovering (ongoing grade 2 symptoms) at the time of the data cut

## KEY TAKEAWAY

At a median follow-up of 28 months, patients treated with cilta-cel showed durable and deepening responses, with median PFS and OS not yet reached and a manageable safety profile

## CONCLUSIONS

- The ORR to cilta-cel remained at 98%, with 83% of patients achieving sCR with longer follow-up
- The safety profile was manageable with a favorable risk-benefit profile and one new case of parkinsonism (day 914 after cilta-cel) since the last report
- Cilta-cel is currently under further investigation in patients with MM in earlier-line settings in CARTITUDE-2, CARTITUDE-4, CARTITUDE-5, *EM*agine/CARTITUDE-6[7]
- Cilta-cel (CARVYKTI™) has been approved in the US for patients with ≥4 prior LOT[3] and will help fill an unmet need in this difficult-to-treat population


### ACKNOWLEDGMENTS

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### DISCLOSURES

**Saad Z Usmani** has served in a consulting or advisory role for AbbVie, Amgen, Array Biopharma, BMS, Celgene, GlaxoSmithKline, Janssen, Merck, Sanofi, Seattle Genetics, SkylineDX, and Takeda Pharmaceuticals, has received speaking fees from Amgen, Janssen, and Takeda, has received honoraria from Amgen, BMS, Celgene, Janssen, Pharmacyclics, Sanofi, and Takeda Pharmaceuticals, and has received research funding from Amgen, Array Biopharma, BMS, Celgene, GlaxoSmithKline, Incyte, Janssen, Merck, Pharmacyclics, Sanofi, Seattle Genetics, SkylineDX, and Takeda Pharmaceuticals. **Thomas Martin** has received research funding from Janssen. **Jesus G Berdeja** has served in a consulting or advisory role for Amgen, Bioclinica, BMS, Celgene, CRISPR Therapeutics, Janssen, Karyopharm, Kite Pharma, Legend, Prothena, Servier, and Takeda Pharmaceuticals, and has received research funding from AbbVie, Acetylon, Amgen, Bluebird, BMS, Celgene, Cellularity, Constellation, CRISPR Therapeutics, CURIS, EMD Serono, Genentech, Inc., Glenmark, Janssen, Kesios, Lilly, Novartis, Poseida, Takeda Pharmaceuticals, Teva, and Vivolux. **Andrzej Jakubowiak** has served in a consulting or advisory role for AbbVie, Adaptive, Amgen, BMS, Celgene, GlaxoSmithKline, Janssen, Juno, Karyopharm, and Sanofi and received honoraria from AbbVie, Adaptive, Amgen, BMS, Celgene, GlaxoSmithKline, Janssen, Juno, Karyopharm, and Sanofi. **Mounzer Agha** has no financial conflicts to disclose. **Adam D Cohen** has received research funding from GlaxoSmithKline and Novartis and has served in a consulting or advisory role for AstraZeneca, BMS/Celgene, Genentech/Roche, GlaxoSmithKline, Janssen, Oncopeptides, and Takeda Pharmaceuticals. **Abhinav Deol** has served in a consulting or advisory role for Adicet Therapeutics, Janssen, Kite, a Gilead Company, and Novartis. **Myo Htut** has no financial conflicts to disclose. **Alexander Lesokhin** has received research funding from BMS, Genentech, and Janssen, has served in a consulting or advisory role for BMS, GenMab, Juno, and Takeda Pharmaceuticals, has received honoraria from BMS, GenMab, Juno, and Takeda Pharmaceuticals, and has royalties from patents from Serametrix Inc. **Nikhil C Munshi** has served in a consulting or advisory role for Amgen, BMS, Celgene, AbbVie, Janssen, Karyopharm, Legend, Novartis, Pfizer, Oncopeptides, Raqia, and Takeda Pharmaceuticals. **Elizabeth O'Donnell** has no financial conflicts to disclose. **Carolyn C Jackson** is employed by Janssen and is a consultant physician at the Memorial Sloan Kettering Cancer Center. **Tzu-min Yeh, Arnob Banerjee, Enrique Zudaire**, and **Deepu Madduri** are employed by Janssen. **Changwei Zhou** and **Lida Pacaud** are employed by Legend Biotech. **Yi Lin** has received research funding from Bluebird Bio, Celgene, Janssen, Kite, a Gilead Company, Merck, and Takeda Pharmaceuticals, has served in a consulting or advisory role for Bluebird Bio, Celgene, Gamida Cells, Janssen, Juno/BMS, Kite, a Gilead Company, Novartis, Sorrento, and Vineti. **Sundar Jagannath** has served in a consulting or advisory role for BMS, Janssen, Karyopharm Therapeutics, Merck, Sanofi, and Takeda Pharmaceuticals.


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